General

Guideline Title

Nystagmus and oscillopsia.

Bibliographic Source(s)

Straube A, Bronstein A, Straumann D, European Federation of Neurologic Societies. Nystagmus and oscillopsia. Eur J Neurol. 2012 Jan;19(1):6-14. [101 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Straube A, Leigh RJ, Bronstein A, Heide W, Riordan-Eva P, Tijssen CC, Dehaene I, Straumann D. EFNS task force--therapy of nystagmus and oscillopsia. Eur J Neurol 2004 Feb;11(2):83-9.

Recommendations

Major Recommendations

The levels of evidence (class I-IV) supporting the recommendations and ratings of recommendations (A-C) are defined at the end of the "Major Recommendations" field.

All treatment recommendations are classified as Class C.

Supranuclear Ocular Motor Disorders

Downbeat Nystagmus (DBN)

No studies on the natural course of DBN are available. In non-placebo-controlled-studies with a limited number of patients, administration of the gamma-aminobutyric acid (GABA)-A agonist clonazepam (0.5 mg per os [p.o.] three times daily) (Currie & Matsuo, 1986), the GABA-B agonist baclofen (10 mg p.o. three times daily) (Dieterich et al., 1991), and gabapentin (probably calcium channel blocker) (Averbuch-Heller et al., 1997) had positive effects and reduced DBN. Intravenous injection of the cholinergic drug physostigmine (acetylcholine [Ach]-esterase inhibitor) worsened DBN in five patients. This effect was partially reversed in one patient by the anticholinergic drug biperiden, suggesting that anticholinergic drugs might be beneficial, as was shown in a double-blind study on intravenous scopolamine (Barton, Huaman, & Sharpe, 1994). In isolated patients with a craniocervical anomaly, a surgical decompression by removal of part of the occipital bone in the region of the foramen magnum was beneficial (Pedersen et al., 1980; Spooner & Baloh, 1981; Liebenberg et al., 2005; personal observation). Recent placebo-controlled studies have suggested that the potassium channel blockers 3,4-diaminopyridine (3 x 20 mg/day) and 4-aminopyridine (3 x 10 mg/day) may be effective in reducing DBN (Strupp et al., 2003) and in improving the vestibulo-ocular reflex (VOR) and smooth pursuit (Kalla et al., 2004). A further study in

11 patients with DBN because of cerebellar degeneration confirmed this effect and showed that 3,4-diaminopyridine especially reduce the gravity-independent velocity bias (Sprenger et al., 2006). As DBN is generally less pronounced in upward gaze, base-down prisms sometimes help to reduce oscillopsia during reading in some patients.

Upbeat Nystagmus

Treatment with baclofen (5–10 mg p.o. three times daily) resulted in an improvement in several patients (Dieterich et al., 1991). There are some observations that 10 mg 4-aminopyridine three times a day reduces upbeat nystagmus (Glasauer et al., 2005).

Seesaw Nystagmus

Alcohol had a beneficial effect (1.2 g/kg body weight) in two patients (Frisèn & Wikkelso, 1986; Lepore, 1987), but this cannot be recommended as treatment, as did clonazepam (Carlow, 1986). Recently, Averbruch-Heller et al. (1997) reported on three patients with a seesaw component to their pendular nystagmus, who improved on gabapentin.

Periodic Alternating Nystagmus (PAN)

In general, PAN does not improve spontaneously. Several case reports of acquired as well as congenital PAN describe a positive effect of baclofen, a GABA-B agonist, in a dose of 5–10 mg p.o. three times daily (Carlow, 1986; Halmagyi, Rudge, & Gresty, 1980; Larmande & Larmande, 1983; Isago, Tsuboya, & Kataura, 1985; Nuti et al., 1986; Comer, Dawson, & Lee, 2006). Furthermore, phenothiazine and barbiturates have been found to be effective in single cases (Isago, Tsuboya, & Kataura, 1985; Nathanson, Bergman, & Bender, 1953). Recently, also memantine was described as effective (Kumar et al., 2009). PAN because of bilateral visual loss resolves if vision is restored (Cross, Smith, & Norton, 1982; Jay, Williams, & De Chicchis, 1985). In a case of PAN associated to a Chiari-malformation, a surgical decompression resolved the PAN (Al-Awami et al., 2005).

Non-vestibular Supranuclear Ocular Motor Disorders

Acquired Pendular Nystagmus (APN)

Most reports (case reports or case series) state that anticholinergic treatment with trihexyphenidyl (20–40 mg p.o. daily) is effective (Herishanu, & Louzoun, 1986; Jabbari et al., 1987), but in a double-blind study by Leigh et al. (1991), only one of six patients showed improvement from this oral treatment, whereas three patients showed a decrease in nystagmus and improvement of visual acuity during treatment with tridihexethyl chloride (a quaternary anticholinergic that does not cross the blood–brain barrier). In contrast, Barton et al. (1994) found in a double-blind trial that scopolamine (0.4 mg intravenous [i.v.]) decreased the nystagmus in all five tested patients with APN. However, there are even observations that scopolamine may make the pendular nystagmus worse in some patients (Kim, Averbuch-Heller, & Leigh, 2001). In three other patients, the combination with lidocaine (100 mg i.v.) decreased nystagmus (Gresty, Ell, & Findley, 1982; Ell et al., 1982). Recently, Starck et al. (1997) reported an improvement in three of 10 patients who received a scopolamine patch (containing 1.5 mg scopolamine, released at a rate of 0.5 mg/day). The same authors failed to observe further improvement when scopolamine and mexiletine (400–600 mg p.o. daily) were given in combination. The most effective substance in their study was memantine, a glutamate antagonist, which significantly improved the nystagmus in all nine tested patients (15–60 mg p.o. daily). Two patients responded to clonazepam (3 x 0.5–1.0 mg p.o. daily), a GABA-A agonist (Starck et al., 1997). In a further crossover study, Starck and coworkers (2010) showed that memantine as well as gabapentin was able not only to reduce the nystagmus but also to improve visual acuity. Two other groups have reported benefit with GABA-ergic drugs. Traccis et al. (1990) showed improvement in one of three patients with APN and cerebellar ataxia because of multiple sclerosis (MS) when treated with isoniazid (800–1000 mg p.o. daily) and glasses with prisms that induced convergence. This observation was not confirmed by other investigators (Leigh et al., 1994). Gabapentin substantially improved the nystagmus (and visual acuity) in 10 of 15 patients (Averbuch-Heller et al., 1997). Gabapentin was superior to vigabatrin in a small series of patients (Bandini et al., 2001). Interestingly, Mossman et al. (1993) described two patients who benefited from intake of alcohol but not from other substances. Recently, a beneficial effect of cannabis was also reported (Schon et al., 1999; Dell'Osso, 2000).

Practically, treatment should start with memantine in a dosage of 15–60 mg p.o. or alternatively 300–400 mg gabapentin three times daily. If there is no or only a small effect, benzodiazepines like clonazepam (0.5–1.0 mg p.o. three times daily) can be tried. Further possibilities are scopolamine patches or trihexyphenidyl.

Opsoclonus and Ocular Flutter

In addition to therapy for any underlying process such as tumour or encephalitis, treatment with immunoglobulins or prednisolone may be occasionally effective (Pless & Ronthal, 1996). Four of five patients with square-wave oscillations, probably a related fixation disturbance, showed an improvement on therapy with valproic acid (Traccis et al., 1997) or in patients with hereditary spinocerebellar ataxia on therapy with memantine 20 mg/daily (Serra et al., 2008). In single cases, an improvement has been observed during treatment with propranolol (40–80 mg p.o. three times daily), nitrazepam (15–30 mg p.o. daily) and clonazepam (0.5–2.0 mg p.o. three times daily) (overview in Carlow, 1986; Leopold, 1985).

Nausieda et al. (1981) reported a dramatic improvement in one patient after the administration of 200 mg thiamine i.v.

Congenital Nystagmus

In most cases, therapy is not necessary. Besides surgical interventions (Yee, Baloh, & Honrubia, 1982) only a few reports on medical treatment trials are reported. Baclofen (Pradeep et al., 2008), cannabis (McLean et al., 2007), and especially memantine and gabapentin are described. In a study with 47 patients, memantine (up to 40 mg) as well as gabapentin (up to 2400 mg) were shown to be superior to placebo and both also improved visual acuity (Hertle & Yang, 2006). A similar result was reported in a retrospective study of 23 patients with acquired as well as congenital nystagmus (Shery et al., 2006; Sarvananthan et al., 2006).

Nuclear and Infranuclear Ocular Disorders

Superior Oblique Myokymia

Spontaneous remissions, which can last for days up to years, are typical of superior oblique myokymia but there are several reports that anticonvulsants, especially carbamazepine, have a therapeutic effect. Carbamazepine (200–400 mg p.o. three or four times daily) or, less often, phenytoin (250–400 mg p.o. daily) are recommended (Susac, Smith, & Schatz, 1973; Rosenberg & Glaser, 1983). Gabapentin has also been reported to be effective (Tomsak, Kosmorsky, & Leigh, 2002). Rosenberg and Glaser (1983) described a decrease in the efficacy of the treatment after a month in some patients. Beta-blockers, even topically, have been reported to be effective (Tyler & Ruiz, 1990; Bibby et al., 1994). In chronic cases that did not improve with anticonvulsants, tenotomy of the superior oblique muscle was performed, but usually it necessitates inferior oblique surgery as well (Palmer & Shults, 1984; Brazis et al., 1994). Surgical decompression of the IV nerve has also been reported to be beneficial but may result in superior oblique palsy) (Samii et al., 1998; Scharwey et al., 2000). Practically, treatment should be started with carbamazepine (200–400 mg p.o. three to four times daily) or phenytoin (250–400 mg p.o. daily).

Paroxysmal Vestibular Episodes

As initial therapy, an anticonvulsant should be given (Brandt, 1999). Mean dosages of carbamazepine of about 600 mg/day and of oxcarbazepine of about 900 mg/day led to a reduction in the attack frequency of about 90% (Scharwey et al., 2000). In general, a positive response to antiepileptic drugs can be achieved with low dosages. If the symptoms do not cease, a surgical approach may be considered (Jannetta, Møller, & Møller, 1984). There are no satisfactory follow-up studies, and the diagnostic criteria have not yet been fully established.

Definitions:

Evidence Classification Scheme for a Therapeutic Intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

a. Randomization concealment
b. Primary outcome(s) is/are clearly defined
c. Exclusion/inclusion criteria are clearly defined
d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
e. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

Rating of Recommendations for a Therapeutic Intervention

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Nystagmus and oscillopsia

Guideline Category

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Neurology

Ophthalmology

Intended Users

Physicians

Guideline Objective(s)

To summarize all published treatment options for nystagmus and oscillopsia as well as to provide a short overview on definitions and pathomechanisms of certain distinct ocular motor syndromes

Target Population

Patients presenting with nystagmus and oscillopsia

Interventions and Practices Considered

1. Benzodiazepines (e.g., clonazepam, nitrazepam)
2. Baclofen
3. Anticonvulsants (e.g., carbamazepine, oxcarbazepine, phenytoin, valproic acid, gabapentin)
4. Anticholinergic drugs (e.g., biperiden)
5. 3,4-diaminopyridine
6. 4-aminopyridine
7. Phenothiazine
8. Barbiturates

9. Memantine
10. Antimuscarinics (e.g., scopolamine [with and without lidocaine], trihexyphenidyl, tridihexethyl chloride)
11. Isoniazid (in patients with multiple sclerosis)
12. Immunoglobulins
13. Prednisolone
14. Beta-blockers (e.g., propranolol)
15. Intravenous thiamine
16. Cannabis
17. Surgical treatment (decompression, tenotomy of the superior oblique muscle)
18. Base-down prisms
19. Glasses with prisms
20. Therapy for any underlying process for opsoclonus and ocular flutter

Major Outcomes Considered

Effectiveness of treatment

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

One member of the task force panel searched through all available published information using the database MEDLINE (last search September 2009). The search was restricted to papers published in English, French, or German. The key words used for the search included the following sequences: 'nystagmus and therapy', 'treatment of ocular motor disorders' and 'treatment of double vision'. All published papers were included, as only a limited number of controlled studies are available.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Evidence Classification Scheme for a Therapeutic Intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

Randomization concealment
Primary outcome(s) is/are clearly defined
Exclusion/inclusion criteria are clearly defined
Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias

Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The members of the task force read the first draft of the recommendation and discussed changes (informative consensus approach).

Most drug treatments are based on case reports. Only recently several small controlled trials have been published, and they were all based on a small number of subjects, and not all patients always respond positively to the treatment. Thus, all treatment recommendations have to be classified as Class C.

Rating Scheme for the Strength of the Recommendations

Rating of Recommendations for a Therapeutic Intervention

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Peer Review

Description of Method of Guideline Validation

The guidelines were validated according to the European Federation of Neurological Societies (EFNS) criteria (see the "Availability of Companion Documents" field).

Evidence Supporting the Recommendations

References Supporting the Recommendations

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Type of Evidence Supporting the Recommendations

Most drug treatments are based on case reports. Only recently several small controlled trials have been published, and they were all based on a small number of subjects.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate therapy of nystagmus and oscillopsia

Potential Harms

- Surgical decompression of the IV nerve for superior oblique myokymia has been reported to be beneficial but may result in superior oblique palsy.
- There are observations that scopolamine may make the pendular nystagmus worse in some patients.

Qualifying Statements

Qualifying Statements

This guideline provides the view of an expert task force appointed by the Scientific Committee of the European Federation of Neurological Societies (EFNS). It represents a peer-reviewed statement of minimum desirable standards for the guidance of practice based on the best available evidence. It is not intended to have legally binding implications in individual cases.

Implementation of the Guideline

Description of Implementation Strategy

The European Federation of Neurological Societies has a mailing list and all guideline papers go to national societies, national ministries of health, World Health Organisation, European Union, and a number of other destinations. Corporate support is recruited to buy large numbers of reprints of the guideline papers and permission is given to sponsoring companies to distribute the guideline papers from their commercial channels, provided there is no advertising attached.

Implementation Tools

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Straube A, Bronstein A, Straumann D, European Federation of Neurologic Societies. Nystagmus and oscillopsia. Eur J Neurol. 2012 Jan;19(1):6-14. [101 references] PubMed

Adaptation

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Guideline Committee

European Federation of Neurological Societies Task Force on Nystagmus and Oscillopsia

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Guideline Availability

Electronic copies: Available to registered users from the European Federation of Neurological Societies Web site .

Availability of Companion Documents

The following are available:

- Brainin M, Barnes M, Baron JC, Gilhus NE, Hughes R, Selmaj K, Waldemar G; Guideline Standards Subcommittee of the EFNS Scientific Committee. Guidance for the preparation of neurological management guidelines by EFNS scientific task forces – revised recommendations 2004. Eur J Neurol. 2004 Sep;11(9):577-81. Electronic copies: Available in Portable Document Format (PDF) from the European Federation of Neurological Societies (EFNS) Web site .
- Continuing Medical Education questions are available to registered users from the EFNS Web site .

Patient Resources

None available

NGC Status

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